

Claims:

1. A method of assessing an individual for a cancer condition comprising;

5 providing a tissue sample obtained from said individual,

determining the presence in said sample of one or more cells comprising a plexinB1 nucleic acid sequence having one or more mutations therein,

10 the presence of said one or more cells being indicative of said individual having a cancer condition.

2. A method according to claim 1 wherein said one or more mutations alter the expression and/or activity of a plexin polypeptide encoded by said nucleic acid.

3. A method according to any one of the preceding claims wherein said one or more mutations are in a non-coding region of said plexin nucleic acid.

20 4. A method according to claim 1 or claim 2 wherein said one or more mutations are in a coding region of said plexin nucleic acid.

25 5. A method according to claim 4 wherein said plexin nucleic acid sequence encodes a plexinB1 polypeptide having one or more mutations therein.

30 6. A method according to claim 5 wherein the plexin B1 polypeptide comprises one or more mutations in the cytoplasmic domain thereof.

7. A method according to claim 5 or claim 6 wherein the one or more mutations are at one or more mutation sites selected from the group consisting of T1697, T1733, T1776, T1795, T1802, P1597, P1798, F1711, G1602, L1815, N1735,
5 R1904, A1730, G1728, and K1613.

8. A method according to claim 7 wherein the one or more mutations are selected from the group consisting of T1697A, T1733I, T1776A, T1795A, T1802A, P1597L, P1597S, P1798S,
10 F1711I, G1602T, L1815P, N1735S, R1904W, A1730T, G1728S, L1815F, and K1613E.

9. A method according to claim 8 wherein the polypeptide comprises a mutation selected from the group consisting of
15 T1795A, P1597S, P1597L, and L1815P.

10. A method according to claim 8 wherein the polypeptide comprises the mutation T1795A.

20 11. A method according to any one of the preceding claims wherein the cancer condition is prostate cancer or breast cancer.

12. A method according to any one of claims 1 to 11
25 wherein the presence of said one or more cells is determined by detecting the presence of said plexinB1 polypeptide.

13. A method of determining the invasiveness of a cancer
30 cell in a sample obtained from an individual, the method comprising,

determining the presence or absence in said cell of a plexin B1 polypeptide having one or more mutations therein,

REPLACED BY
ART 34 AMDT

the presence of said plexin B1 polypeptide being indicative that the cell is invasive.

14. A method according to claim 13 wherein said one or
5 more mutations alter the expression and/or activity of a plexin polypeptide encoded by said nucleic acid.

15. A method according to claim 13 or claim 14 wherein
10 said one or more mutations are in a non-coding region of said plexin nucleic acid.

16. A method according to claim 13 or claim 14 wherein
15 said one or more mutations are in a coding region of said plexin nucleic acid.

17. A method according to claim 16 wherein said plexinB1
nucleic acid sequence encodes a plexinB1 polypeptide having
one or more mutations therein.

20 18. A method according to claim 17 wherein the plexinB1
polypeptide comprises one or more mutations in the
cytoplasmic domain thereof.

19. A method according to claim 17 or claim 18 wherein the
25 one or more mutations are at one or more mutation sites
selected from the group consisting of T1697, T1733, T1776,
T1795, T1802, P1597, P1798, F1711, G1602, L1815, N1735,
R1904, A1730, G1728, and K1613.

30 20. A method according to claim 19 wherein the one or more
mutations are selected from the group consisting of T1697A,
T1733I, T1776A, T1795A, T1802A, P1597L, P1597S, P1798S,

F1711I, G1602T, L1815P, N1735S, R1904W, A1730T, G1728S,
L1815F, and K1613E.

21. A method according to claim 20 wherein the polypeptide
5 comprises a mutation selected from the group consisting of
T1795A, P1597L, P1597S, and L1815P.

22. A method according to claim 19 wherein the polypeptide
comprises the mutation T1795A.

10

23. A method according to any one of the preceding claims
wherein the cancer condition is prostate cancer or breast
cancer.

15 24. A method according to any one of claims 13 to 23
wherein the presence of said one or more cells is
determined by detecting the presence of said plexinB1
polypeptide.

20 25. A method of identifying and/or obtaining a putative
anti-cancer agent, the method comprising;
contacting a plexinB1 polypeptide with a test compound
and;

determining the activity of the plexinB1 polypeptide
25 in the presence relative to the absence of test compound.

26. A method according to claim 25 wherein plexin
polypeptide comprises one or more mutations.

30 27. A method according to claim 26 wherein the one or more
mutations are in the cytoplasmic domain of the plexinB1
polypeptide.

28. A method according to claim 27 wherein the one or more mutations are at one or more mutation sites selected from the group consisting of T1697, T1733, T1776, T1795, T1802, P1597, P1798, F1711, G1602, L1815, N1735, R1904, A1730,
5 G1728, and K1613.

29. A method according to claim 28 wherein the one or more mutations are selected from the group consisting of T1697A, T1733I, T1776A, T1795A, T1802A, P1597L, P1597S, P1798S,
10 F1711I, G1602T, L1815P, N1735S, R1904W, A1730T, G1728S, L1815F, and K1613E.

30. A method according to any one of claims 25 to 29 wherein the plexinB1 polypeptide is expressed on the
15 surface of a cell

31. A method according to claim 30 wherein the activity is plexinB1-mediated anchorage independent growth of said cell.
20

32. A method according to any one of claims 25 to 30 wherein the activity of the plexinB1 polypeptide is determined by determining the binding of said polypeptide to one or more of semaphorin4D, active Rac1, neuropilin,
25 PDZ-RhoGEF and LARG and other components of the semaphorin signalling pathway interacting with plexinB1.

33. A method according to any one of claims 25 to 30 wherein the activity of the plexinB1 polypeptide is
30 determined by determining the activation of Rho GTPase.

34. A method according to any one of claims 26 to 30 comprising the further step of;

contacting a wild-type plexinB1 polypeptide with the test compound, and;

determining the activity of the wild-type plexinB1 polypeptide.

5

35. A method according to any one of claims 26 to 30 comprising the further steps of;

contacting the mutant plexinB1 polypeptide with the test compound in the presence of a wild-type plexinB1, and;

10 determining the activity of the wild-type plexinB1 polypeptide.

36. A method of identifying and/or obtaining a compound as a putative anti-cancer agent, the method comprising;

15 contacting a plexinB1 nucleic acid with a test compound and;

determining the expression of the plexinB1 nucleic acid in the presence relative to the absence of test compound.

20 37. A method according to claim 36 wherein the plexinB1 nucleic acid comprises one or more mutations.

38. A method according to claim 37 wherein one or more mutations are in a non-coding region of the nucleic acid.

25

39. A method according to claim 37 wherein the one or more mutations are in a coding region of the nucleic acid.

40. A method according to claim 39 wherein the one or more mutations are in a region of the nucleic acid which encodes the cytoplasmic domain of the plexinB1 polypeptide.

30

41. A method according to claim 40 wherein the one or more mutations are at one or more mutation sites selected from the group consisting of 5059, 5060, 5074, 5107, 5359, 5401, 5452, 5458, 5468, 5474, 5596, 5653, 5662, 5674, 5713, 5714, and 5980 of the plexinB1 coding sequence.

42. A method according to claim 42 wherein the one or more mutations are selected from the group consisting of C5059T, C5060T, G5074A, A5107G, A5359G, T5401A, G5452A, G5458A, T5468C, A5474G, A5596G, A5653G, C5662T, A5674G, C5713T, T5714C and C5980T.

43. A method according to claim 36 comprising determining the increase in the expression of wild-type plexin B1 in the presence of said test compound.

44. A method according to any one of claims 36 to 41 comprising determining the decrease in the expression of mutant plexin B1 in the presence of said test compound

20

45. A method according to any one of claims 26 to 44 comprising identifying the test compound as a putative anti-cancer agent.

25 46. A method according to claim 45 comprising isolating and/or purifying the test compound.

47. A method according to claim 46 comprising modifying the test compound to optimise its pharmaceutical properties.

30

48. A method according to any one of claims 45 to 47 comprising formulating said test compound with a pharmaceutically acceptable excipient.

5 49. A method of producing a pharmaceutical compound comprising the steps of;
identifying a compound using any one of claims 25-47 and;
formulating said test compound with a pharmaceutically acceptable excipient.

10

50. A compound identified as a putative anti-cancer agent by a method of claim 45.

15

51. A pharmaceutical composition comprising the compound of claim 50 and a pharmaceutically acceptable excipient.

52. A compound according to claim 50 for use in a method of treatment

20

53. Use of a compound according to claim 50 in the manufacture of a medicament for use in the treatment of cancer.

25

54. A nucleic acid encoding plexinB1 or its complement or a fragment thereof for use in a method of treatment.

55. A nucleic acid encoding mutant plexinB1 polypeptide or its complement or a fragment thereof for use in a method of treatment.

30

56. A nucleic acid according to claim 55 wherein the mutant plexinB1 polypeptide has one or more mutations in the cytoplasmic domain.

57. A nucleic acid according to claim 56 wherein the one or more mutations are at one or more mutation sites selected from the group consisting of T1697, T1733, T1776,
5 T1795, T1802, P1597, P1798, F1711, G1602, L1815, N1735, R1904, A1730, G1728, and K1613.

58. A nucleic acid according to claim 57 wherein the one or more mutations are selected from the group consisting of
10 T1697A, T1733I, T1776A, T1795A, T1802A, P1597L, P1597S, P1798S, F1711I, G1602T, L1815P, N1735S R1904W, A1730T, G1728S, L1815F, and K1613E

59. A nucleic acid according to any one of claims 54 to 58
15 for use in a method of treating cancer.

60. Use of nucleic acid encoding plexinB1 or its complement or a fragment thereof in the manufacture of a medicament for the treatment of cancer.

20 61. Use of nucleic acid encoding mutant plexinB1 or its complement or a fragment thereof in the manufacture of a medicament for the treatment of cancer.

25 62. Use according to claim 61 wherein the mutant plexinB1 polypeptide has one or more mutations in the cytoplasmic domain.

30 63. Use according to claim 61 wherein the one or more mutations are at one or more mutation sites selected from the group consisting of T1697, T1733, T1776, T1795, T1802, P1597, P1798, F1711, G1602, L1815, N1735, R1904, A1730, G1728, and K1613.

64. Use according to claim 63 wherein the one or more mutations are selected from the group consisting of T1697A, T1733I, T1776A, T1795A, T1802A, P1597L, P1597S, P1798S, F1711I, G1602T, L1815P, N1735S, R1904W, A1730T, G1728S, L1815F and K1613E.

65. A method of treating a cancer condition in an individual, the method comprising introducing nucleic acid according to claims 60-64 in to one or more cells of said individual.

66. A method of screening for an antibody molecule specific for a mutant plexinB1, the method comprising; providing a population of antibody molecules specific for mutant plexinB1, contacting said population with a normal plexinB1 polypeptide, identifying one or more members of said population which bind preferentially to mutant plexinB1 relative to normal plexinB1.

67. A antibody molecule which specifically binds to a mutant plexinB1 polypeptide.

68. A method of treating a cancer condition in an individual, the method comprising reducing the activity of mutant plexinB1 polypeptide in one or more cells of said individual.

69. A method according to claim 68 wherein the activity of mutant plexinB1 polypeptide is reduced by administering an antagonist of mutant plexinB1 to said individual.

REPLACED BY
ART 34 AMEND

70. A method according to claim 68 wherein the activity of mutant plexinB1 polypeptide is reduced by decreasing or abolishing expression of the mutant plexin B1 polypeptide.

5

71. A method according to claim 68 wherein expression of the mutant plexin B1 polypeptide is abolished or reducing by administering a nucleic acid according to any one of claims 53 to 58.

10

72. A method of reducing the invasiveness of a tumour in an individual comprising reducing the activity of mutant plexinB1 polypeptide in one or more cells of said tumour.

15

73. A method according to claim 72 wherein the activity of mutant plexinB1 polypeptide is reduced by administering an antagonist of mutant plexinB1 to said individual.

20

74. A method according to claim 72 wherein the activity of mutant plexinB1 polypeptide is reduced by decreasing or abolishing expression of a mutant plexinB1 polypeptide.

25

75. A method according to claim 72 wherein expression of a mutant plexin B1 polypeptide is abolished or reducing by administering a nucleic acid according to any one of claims 53 to 58.